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Original qualitative research

Vaping-associated lung illness (VALI) in Canada: a descriptive analysis of VALI cases reported from September 2019 to December 2020

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Abstract

Introduction: The aim of this study was to explore demographic and clinical characteristics of vaping-associated lung illness (VALI) cases reported in Canada from September 2019 to December 2020; compare the epidemiology of VALI cases in Canada to e-cigarette or vaping product use-associated lung injury (EVALI) cases in the US; and examine possible explanations for differences between the two countries.

Methods: A federal/provincial/territorial task group developed a national outbreak definition, minimum dataset and case report form for identification and surveillance of VALI cases in Canada. Descriptive analysis explored the characteristics and epidemiology of reported VALI cases.

Results: Of the 20 VALI cases reported, none resulted in a death. Of all cases, 5 (25%) involved youth aged 15 to 19 years, 10 (50%) adults aged 20 to 49 years and 5 (25%) aged 50 years and older. Sixty percent of patients were men. Half (50%) required breathing assistance. Three-quarters (75%) reported using nicotine-containing vaping products, and 40% reported use of cannabis-containing vaping products; of those who reported frequency of vaping, most (71%) reported vaping daily. VALI cases were reported at a lower prevalence (0.9 per million) than EVALI (8.5 per million). Demographics and vaping behaviour also differed.

Conclusion: VALI cases were reported in Canada between September 2019 and December 2020; however, there was a much lower prevalence and they may have been caused by different factors from the EVALI outbreak in the US. The factors influencing VALI in Canada are complex and multifactorial. Research is needed to understand the short- and long-term health effects of nicotine and cannabis vaping.

Keywords: *e-cigarette use, electronic cigarette, nicotine vaping, tetrahydrocannabinol (THC), cannabis vaping, lung illness, lung injury, vape*

Highlights

- In Canada, the use of e-cigarettes has been increasing, particularly among youth.
- Between September 2019 and December 2020, 20 cases of vaping-associated lung illness (VALI) were reported in Canada.
- Canada experienced a lower per-population prevalence of VALI compared to e-cigarette or vaping product use-associated lung injury (EVALI) in the US; differences in patient demographics and products used were also found.

Introduction

In Canada, the use of electronic cigarettes (e-cigarettes or vaping devices) has been increasing, particularly among youth. Between 2015 and 2019, the number of Canadians aged 15 years and older who reported ever-vaping (nicotine) increased from 13% to 16%,[1,2] with younger age groups reporting the highest frequency: 36% of youth aged 15 to 19 years and 48% of young adults (20 to 24 years), compared to 12% of adults (25 years and over) in 2019.[2] Among students in grades 7 to 12 in Canada, 20% reported past- 30-day use of e-cigarettes in 2018-2019, double the number of students who reported past 30-day use in 2016-2017 (10%).[1,3]

Similar findings were reported in 2019: past 30-day use of a vaping device was higher among youth and young adults (15% each, respectively) compared to adults (3%) in Canada.[2] Ever-vaping cannabis-containing products was reported by 9% of Canadians 15 years of age and older in 2019; past 30-day use was reported by 3% of Canadians, with young adults (7%) reporting past 30-day use more than youth and adults (3% each, respectively).[2]

E-cigarettes and vaping products have been marketed as a potentially less harmful alternative to combustible products; however, long-term risks, both acute and chronic, remain mostly unknown.[4] The exposure to potentially harmful chemicals while vaping is variable and depends on the composition of the vaping liquid or product, the legal status and source of

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product and how the product is used. Across both nicotine-containing and cannabis-containing vaping products in the United States, more than 500 chemicals have been identified in vaping cartridges and liquids, including various amounts of nicotine, cannabinoids, volatile organic compounds, vitamin E acetate, silicon conjugated compounds and various terpenes, metals and pesticides.[5,6]

In August 2019, the US Centers for Disease Control and Prevention (CDC) reported an outbreak of e-cigarette or vaping product use-associated lung injury (EVALI). At the request of the Chief Public Health Officer of Canada, the Public Health Agency of Canada (PHAC) alerted provincial and territorial health authorities of the potential for cases and the need for enhanced vigilance.

Studies of EVALI cases in the US have examined the common factors and clinical features associated with EVALI; however, no specific substance, product or device was linked to all cases. Nonetheless, vitamin E acetate, an additive found in cannabis products (and typically not in nicotine products) from informal sources such as friends, family and the illegal market was found to be strongly linked to the EVALI outbreak in the US; 82% of EVALI patients reported using cannabis-containing vaping products, of which 78% reported acquiring these products from informal sources. However, evidence was not sufficient to rule out the contribution of other chemicals found in any vaping product whether cannabis-containing or not, as EVALI occurred among those who did not report vaping cannabis-containing products.[7-9]

The severity and nonspecificity of vaping-associated lung illness (VALI) symptoms present a diagnostic challenge for physicians, particularly if a patient does not disclose having recently vaped. Patients who might have VALI may visit primary care clinics or outpatient hospital emergency services, and treatment can vary from hospital or intensive care unit (ICU) admission, to being placed on a regimen of antibiotics or steroids, to receiving supplementary oxygen or ventilation, or even to being placed on life support.[10] Exploring trends in VALI cases in Canada contributes to the evidence base for improved understanding of severe vaping-related harms and clinical management of suspected VALI cases. Accordingly, the objectives of this study were to (1) explore the demographic and clinical patient characteristics in VALI cases reported in Canada from September 2019 to December 2020; (2) compare the epidemiology of VALI in Canada to EVALI in the US; and (3) examine possible explanations for the differences in the epidemiology between Canada and the US.

Methods

Case data

To coordinate a national investigation, in September 2019, the Canadian Council of Chief Medical Officers of Health (CCMOH) approved the formation of the federal, provincial and territorial (F/P/T) VALI Task Group to develop a common approach to detect, investigate and report on cases of VALI in their respective jurisdictions. The F/P/T VALI Task Group created data collection tools, a national outbreak case definition for severe pulmonary disease associated with vaping or dabbing (Table 1), a minimum dataset for standardized data collection and a case report form. "Vaping" is the act of inhaling an aerosol produced by a vaping product. "Dabbing" is inhaling very hot vapours from heated cannabis oils, concentrates or extracts.

Self-reported vaping behaviours were obtained during initial and follow-up interviews with either the patient or close family members, if the patient was unable to participate. Provincial and territorial (P/T) public health authorities submitted de-identified case data to PHAC after a VALI case was verified as probable or confirmed against the national case definition in their jurisdiction. Health Canada (HC) also actively searched existing databases for self-reported and industry-reported adverse reactions to nicotine, non-nicotine and cannabis vaping products, and e-cigarette or vaping devices. Four possible incidents of lung injury related to vaping in Canada were identified and shared with PHAC.

Investigative efforts and reporting in Canada focussed on hospitalized patients, using a similar case definition and strategy as the US investigation; however, Alberta, British Columbia, New Brunswick and Quebec expanded their investigations to include outpatient visits and family physician settings. In March 2020, when COVID-19 transmission became widespread in Canada, active surveillance of VALI was paused and surveillance was limited to monitoring and reporting adverse reactions and to incidents event reporting through existing HC regulatory surveillance programs. Characteristics of EVALI cases were sourced from public health data and published literature. This study, which covered the reporting period of September 2019 to December 2020, and this paper were approved by the F/P/T VALI Task Group of the CCMOH. Ethics approval was not required, as this study falls within routine public health surveillance activities.

Laboratory testing

Health Canada's Regulatory Operations and Enforcement Branch Laboratories (HC-ROEB-Laboratories) conducted analytical testing of vaping product samples to identify and quantify substances of interest in support of VALI investigations. When possible, patients provided samples of the substances vaped prior to onset of symptoms. HC-ROEB-Laboratories also purchased and tested samples of the same brands that patients reported using, to act as control samples. HC-ROEB-Laboratories carried out the chemical analyses of e-liquids using validated analytical methods employing gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-photodiode array (HPLC-PDA) techniques. Analytes were reported as detected only if their presence in the sample was confirmed by both methods. Health Canada's Healthy Environments and Consumer Safety Branch–Product Safety Laboratory (HC-HECSB-PSL) also provided laboratory services for testing vaping devices linked to cases via visual evaluation, heater coil resistance measurement and testing coils for the presence of heavy metals using a portable x-ray fluorescence analyzer.

Analysis

Given the small number of cases, descriptive analysis was performed using MS Excel spreadsheets that detailed the characteristics and epidemiology of all 20 VALI cases in Canada. Statistical associations and significance tests were not conducted, due to insufficient statistical power resulting from small sample size and the level of availability and completeness of data. Due to low case counts, confirmed and probable cases were combined for analyses.

TABLE 1
Outbreak case definitions of confirmed and probable cases of vaping-associated lung illness (VALI) and e-cigarette or vaping product use-associated lung injury (EVALI)

	Vaping-associated lung illness (VALI)	E-cigarette or vaping product use-associated lung injury (EVALI)
Confirmed	History of vaping or dabbing[a] in the 90 days prior to symptom onset	Using an e-cigarette (vaping) or dabbing[a] in 90 days prior to symptom onset
	AND	AND
	Pulmonary infiltrate, such as opacities, on plain film chest radiograph or ground-glass opacities on chest CT	Pulmonary infiltrate, such as opacities, on plain film chest radiograph or ground-glass opacities on chest CT
	AND	AND
	Absence of pulmonary infection on initial work-up: Minimum criteria are: negative respiratory viral panel, influenza PCR or rapid test, if local epidemiology supports testing. All other clinically indicated respiratory infectious disease testing (e.g. urine antigen for *Legionella*, sputum culture if productive cough, BAL culture if done, blood culture, HIV-related opportunistic respiratory infections if appropriate) must be negative	Absence of pulmonary infection on initial work-up: Minimum criteria are: a negative respiratory viral panel and a negative influenza PCR or rapid test, if local epidemiology supports influenza testing. All other clinically indicated respiratory infectious disease testing (e.g. urine antigen for *Streptococcus pneumoniae* and *Legionella*, sputum culture if productive cough, BAL culture if done, blood culture, HIV-related opportunistic respiratory infections if appropriate) are negative
	AND	AND
	No evidence in medical records of alternative plausible diagnoses (e.g. cardiac, rheumatologic or neoplastic process)	No evidence in medical record of alternative plausible diagnoses (e.g. cardiac, rheumatologic, or neoplastic process)
Probable	History of vaping or dabbing in the 90 days prior to symptom onset	Using an e-cigarette (vaping) or dabbing in 90 days prior to symptom onset
	AND	AND
	Pulmonary infiltrate, such as opacities, on plain film chest radiograph or ground-glass opacities on chest CT	Pulmonary infiltrate, such as opacities, on plain film chest radiograph or ground-glass opacities on chest CT
	AND	AND
	Infection identified via culture or PCR, but clinical team believes this is not the sole cause of the underlying respiratory disease process	Infection identified via culture or PCR, but clinical team believes this infection is not the sole cause of the underlying lung injury
	OR	OR
	Minimum criteria to rule out pulmonary infection not met (testing not performed) and clinical team believes infection is not the sole cause of the underlying respiratory disease process	Minimum criteria to rule out pulmonary infection not met (testing not performed) and clinical team believes infection is not the sole cause of the underlying lung injury
	AND	AND
	No evidence in medical record of alternative plausible diagnoses (e.g. cardiac, rheumatologic or neoplastic process)	No evidence in medical record of alternative plausible diagnoses (e.g. cardiac, rheumatologic, or neoplastic process)

Sources: VALI: Government of Canada. National outbreak case definitions: severe pulmonary disease associated with vaping or dabbing [Internet]. Ottawa (ON): Government of Canada; 2019 [modified 2019 Oct 11; cited 2021 Oct 5]. Available from: https://www.canada.ca/en/public-health/services/diseases/vaping-pulmonary-illness/health-professionals/national-case-definition.html

EVALI: Centers for Disease Control and Prevention (CDC). 2019 lung injury surveillance primary case definitions, September 18, 2019 [Internet]. Atlanta (GA): CDC; 2019 [cited 2021 Oct 05]. Available from: https://www.cdc.gov/tobacco/basic_information/e-cigarettes/assets/2019-Lung-Injury-Surveillance-Case-Definition-508.pdf

Abbreviations: BAL, bronchoalveolar lavage; CT, computed tomography; HIV, human immunodeficiency virus; PCR, polymerase chain reaction.

[a] Inhaling very hot vapours from heated cannabis oils, concentrates or extracts.

Results

During the study period, 20 VALI cases and zero deaths were reported to PHAC by P/T health authorities. Of the 20 VALI cases, 8 were classified as confirmed and 12 as probable, as defined by the national outbreak case definition.

Detailed case information was submitted for 75% (15 of 20 cases) of reported VALI cases in Canada between 1 September 2019 and 31 December 2020.

Data on basic demographics, symptoms, symptom onset, hospitalization status and substance(s) vaped were available for all cases. Detailed information was available for the cases as follows: medical history (13 of 20 cases), medical interventions (13 of 20 cases), source and frequency of substance(s) and devices used for vaping (14 of 20 cases) and use of other substances (combustible or other means of consumption; 16 of 20 cases).

Demographic characteristics

Of all cases, 25% (5 of 20 cases) were among youth aged 15 to 19 years; 50% (10 of 20 cases) were among those aged 20 to 49 years and 25% (5 of 20 cases) were among those aged 50 years and older. Cases were reported in Quebec, British Columbia, Ontario, New Brunswick, Alberta and Newfoundland and Labrador.

Symptoms

Cases reported between 1 September 2019 and 31 December 2020 involved symptom onset dates ranging from 5 May 2019 to 11 April 2020. Half (50%; 10 of 20 cases) had a symptom onset date between August 2019 and October 2019.

All 20 patients reported respiratory symptoms, of which 25% (5 of 20 cases)

reported exclusively respiratory symptoms (e.g. cough, shortness of breath), and 75% (15 of 20 cases) reported a combination of respiratory, gastrointestinal (e.g. nausea, diarrhea), constitutional (e.g. chills, fatigue) and/or other symptoms (e.g. fever, poor appetite/weight loss). Eight patients (40%) reported a fever. Of all 20 patients, 3 (15%) experienced acute respiratory distress syndrome (ARDS). Other symptoms reported included back pain, numbness or tingling, confusion, short-term memory loss, runny nose, sinus pressure, sore throat, sweating, fecal incontinence, lack of balance and urinary symptoms.

By sex, men more commonly reported cough and constitutional symptoms compared to women (cough: 10 of 12 [83%] males compared to 4 of 8 [50%] females; constitutional symptoms: 10 of 12 [83%] males compared to 3 of 8 females [38%]).

Medical history

Detailed case information about pre-existing conditions and other risk factors was available for 65% (13 of 20) of VALI cases. Of those with information available, 62% of patients (8 of 13 cases) reported having one or more pre-existing conditions or risk factors. Of those who reported a pre-existing condition or risk factor, 63% (5 of 8 cases) reported a pre-existing respiratory or lung condition, including asthma and chronic obstructive pulmonary disease (COPD). The majority of patients that reported pre-existing conditions or risk factors (75%; 6 of 8 cases) were aged 40 years and older. No differences were observed in the number of pre-existing conditions or risk factors reported by sex.

Hospitalization and intensive care unit (ICU) admission

Of all 20 VALI patients, 80% (16 of 20 cases) were hospitalized. Detailed case information on date of hospital admission and discharge was available for 14 of the 16 hospitalized patients. The median length of hospitalization was 6 days (range of 2 to 54 days). Of the 14 patients with information available, 86% (12 of 14 cases) were hospitalized for 10 days or less. Of the 16 patients hospitalized, 50% (8 of 16 cases) were admitted to the ICU.

Medical intervention and treatments

Of all 20 VALI patients, 55% (11 of 20 cases) required respiratory intervention. Of the 11 patients who did, 55% (6 of 11 cases) received oxygen support via nasal cannula, while the remaining patients required more intensive or supportive interventions such as ventilation (3 of 11 cases), continuous positive airway pressure (CPAP; 1 of 11 cases) or extracorporeal membrane oxygenation (ECMO; 1 of 11 cases). Additional medical treatments were provided to several patients, including treatment with antimicrobials and/or steroids. A higher percentage of VALI patients aged 40 years or older (6 of 9 cases; 67%) than those VALI patients aged 39 years or younger (5 of 11 cases; 45%) required respiratory interventions. No differences were observed in the type of intervention by sex.

Vaping behaviours

Of all VALI patients, 75% (15 of 20 cases) self-reported having vaped nicotine products. Of these 15 patients, 12 (80%) reported exclusively vaping nicotine products. Seven patients reported vaping nicotine products with flavouring. Most of these reported using more than one flavour (5 of 7 cases). Flavours reported included tobacco (2 cases), fruit (e.g. green apple, strawberry guava, "very berry," and mango, among others; 6 cases) and other flavours (e.g. cotton candy, bubble gum, mint, vanilla; 3 cases). Vaping or dabbing of cannabis-containing products was reported by 40% of all VALI patients (8 of 20 cases). Of these 8 patients, 5 (63%) reported exclusive cannabis vaping (representing a broad category of inhaled substances containing cannabis extracts).

Exclusive nicotine vaping was reported by both men and women in all age groups. Exclusive cannabis vaping use was reported by both men and women less than 60 years of age. Of those who reported vaping using both nicotine- and cannabis-containing products, all were men and under 20 years of age. More women than men (60%; 3 of 5 cases) reported vaping cannabis exclusively, while more men than women (58%; 7 of 12 cases) reported exclusive nicotine vaping.

Different types of devices can be used to vape, creating an inhalable aerosol of nicotine, flavoured substance and/or cannabis extracts; the latter may be in liquid, semi-solid or solid forms (e.g. "shatter," "wax"). Detailed information on type of vaping or dabbing device used was available for 14 of 20 VALI cases. Device types included vape pens with either a tank (refillable), a pre-filled (single use) cartridge, or disposable cartridges. A dab device (dab rig, bong, nail) and other devices were also reported. Most patients (71%; 10 of 14 cases) reported using their device on a daily basis. Information on the amount of substance used each time or how many times each day was not provided. No patients reported using a modified device; however, one reported modifying the vaping substance.

In addition to substances vaped, data on nicotine products and other substances consumed via other means (e.g. inhaled, injected, ingested, combusted) were available for 70% of cases (14 of 20). Of these patients, three-quarters (79%; 11 of 14 cases) reported prior or current combustible tobacco use, while 57% (8 of 14 cases) reported prior or current combustible cannabis use.

Laboratory results of substances and devices

As of 3 June 2020, HC-ROEB-Laboratories had received and analyzed 59 samples related to 8 cases (35 control samples, 16 product samples from patients and 8 samples collected from one patient's device—comprising the substance and swabs of different parts of the device). Vitamin E acetate was detected in one control sample at a very low concentration (0.279 mg/mL). At this concentration, there is no evidence to indicate it could have caused VALI-like symptoms. No specific substance detected or quantified could be pinpointed as a responsible agent for VALI symptoms, based on a risk analysis of the exposure and toxicity information related to samples tested from VALI patients. While the substances that were detected have very low toxicity via the oral route, the inhalation toxicity of most of the substances is currently unknown. Vaping liquid was also tested for the presence of heavy metals such as cadmium, arsenic, lead and mercury. No heavy metals were detected in the liquids tested (Table 2).

HC-HECSB-PSL received 11 devices and evaluated 7 of them. HC-HECSB-PSL's analysis of the devices revealed no key

findings via either visual evaluation or heater coil resistance measurement, and no heavy metals were detected above the limit of detection of the x-ray fluorescent analyzer (< 10 parts per million).

Discussion

From September 2019 to December 2020, 20 VALI cases were reported in Canada, representing a prevalence of 0.9 cases per 1 million population.* As of 18 February 2020, the CDC reported 2807 EVALI cases and 68 deaths in the US, representing a prevalence of approximately 8.5 cases per 1 million population. Given the smaller number of cases in Canada, as well as the differing regulatory and health care systems, it is difficult to compare the characteristics of EVALI in the US with VALI in Canada. While the EVALI outbreak in the US was characterized by a sharp increase in emergency department visits through the summer of 2019 followed by a peak in September 2019,[11] in Canada, a small number of cases (1–4) was reported each month from September 2019 to April 2020.†

Geographically, in the US, EVALI cases were reported by all 50 states, the District of Columbia and two US territories (Puerto Rico and the US Virgin Islands); rates varied by state, with states in the northern Midwest (e.g. Illinois, Minnesota, Indiana) reporting a higher rate of cases than other states.[11,12] Although vaping regulations vary by province, the majority of VALI cases in Canada (80%) were reported in British Columbia, Ontario and Quebec, Canada's three most populous provinces, which account for 75% of the Canadian population. This suggests there is no geographic centre to VALI cases in Canada, as there appears to be the US.

Almost half of all VALI cases in Canada (45%) were among those aged 40 years and older, and there was a higher number of cases among men compared with women (60% male). Comparatively, three-quarters (76%) of US EVALI cases were among those aged 34 years and under, and there was a higher number of men (66%) compared to women;[11] a greater proportion of patients with VALI in Canada are therefore older than those diagnosed with EVALI in the US, while men account for a larger proportion of both VALI and EVALI cases.

TABLE 2
Summary of vaping liquid analysis by HC-ROEB-Laboratories related to VALI cases in Canada, September 2019 to December 2020

Type of vaping liquid sample	Results
Control (n = 35)	**Nicotine** • Present in 22 samples; content is consistent with label claim for all samples • For the remaining 13 samples, nicotine was below the limit of detection; content is consistent with label claim for all samples **Additional substances** • Flavouring agents (e.g. vanillin, benzyl benzoate, benzaldehyde, among others) • Diluents (benzyl alcohol)
Patient (n = 16)	**Nicotine** • Present in 11 samples • Nicotine concentration was consistent with label claim in 6 samples; 5 samples were not large enough to quantify; and in 5 samples, nicotine was not detected (below the limit of detection), which is aligned with label claim **THC** • Present in 4 samples (from 1 patient) **Additional substances** • Vanillin identified in 1 sample
Liquid extracted from patients' devices (n = 8)	**Nicotine** • Present in 8 samples[a]—not enough sample to quantify **Additional substances** • Vanillin identified in 3 samples; traces of cocaine (on the mouthpiece of the vaporizer) identified in 1 sample

Abbreviations: HC-ROEB, Health Canada's Regulatory Operations and Enforcement Branch; THC, tetrahydrocannabinol; VALI, vaping-associated lung injury.

[a] In addition to collecting a sample of the liquid in devices, additional samples were also taken from the device itself by swabbing different components or sections, thus resulting in more samples than the number of devices submitted for testing.

From August to November 2019, approximately 95% of EVALI patients in the US had been hospitalized.[13] Most (80%) VALI patients in Canada were hospitalized; however, this was likely due to case-finding strategies that were limited to hospitalized patients in the majority of the provinces and territories. Expanding the case finding beyond hospitals, as was done by some provinces, led to the detection of additional cases in clinics and emergency departments. It is possible that focussing on hospitalized patients resulted in underreporting of cases that may have involved milder symptoms or were resolved with outpatient interventions, thus not requiring hospitalization.

In Canada, the most common substance vaped by VALI patients was nicotine. In the US, the majority of EVALI patients self-reported using cannabis-containing products obtained from informal sources.[11] For example, 91% of EVALI cases in Minnesota and three patient clusters in Wisconsin (8 cases) involved cannabis-containing vaping products obtained from informal sources such as friends, family or in-person or online dealers, and 75% of THC-containing products reported in California also came from such informal sources.[14-16] In Canada, one VALI patient reported modifying vaping substances, which may have changed the chemistry of the liquid vaped, potentially contributing to adverse effects.[10] Similarly, traces of cocaine detected on one device may indicate the individual was experimenting to produce a different user experience, which may have resulted in adverse health effects. The difference in prevalence between VALI and EVALI cases may be due to the increased proportion of patients reporting vaping cannabis-containing products from informal sources in the US.

More than one potential factor contributing to illness may have been present in Canada at the same time as the US EVALI outbreak. The outbreak of EVALI in the US was strongly associated with vitamin E

* Population estimates were calculated based on Statistics Canada Table 17-10-0009-01, Population estimates, quarterly (2020 Q1). Prevalence is presented per population per year.

† Surveillance is ongoing; additional data and cases may be reported outside the surveillance period included in this report.

acetate added to cannabis-containing vaping products obtained from informal sources;[11,17,18] however, it was not linked to any of the Canadian cases in sufficient amounts. A vitamin E acetate concentration of 0.279 mg/mL (0.03%) was detected in one Canadian control sample; concentrations of 23% to 88% were detected in samples from EVALI cases.[19] Other chemicals that may be present in vaping products cannot be ruled out as contributing factors;[20] furthermore, pre-existing conditions add complexity to case evaluation.

Regulatory differences may have contributed to the differences between case characteristics in Canada and the US as well. Canada's October 2019 legislation regulating inhaled cannabis extracts, including cannabis vaping products, closely restricts additives, carrier ingredients and substances and contaminants (e.g. pesticides and heavy metals) that may pose a risk of injury to human health.[21-23] However, inhaled cannabis extracts frequently used with accessories such as vaping devices did not enter the legal marketplace until December 2019; products used during some of this investigation, prior to December 2019, may not have adhered to these regulations. In the US, there was no federal oversight of these products at the time of the outbreak, requiring each state to develop its own set of regulations and restrictions, resulting in regulations that varied from state to state. States such as Colorado and California, where the adult use of cannabis is legalized, reported lower rates of EVALI cases compared to states where cannabis use is illegal.[24] The variability of product regulations in the US likely did not impact the products used by Canadians, as importation of cannabis-containing products by consumers is prohibited in Canada. Thus the likelihood of adulterated products from the US being legally imported into the Canadian marketplace is reduced.[25]

It is likely that the EVALI outbreak in the US led to increased surveillance and awareness of the potential for vaping-related harms in Canada, which may have contributed to the detection or identification of cases that might not have been reported otherwise or aggregated at the national level.[26-28] Long-established governance structures and relations with the Pan-Canadian Public Health Network, the CCMOH,[29] provincial and territorial health authorities and the media may have expedited timely information sharing, raised awareness and enhanced surveillance of the potential for harm related to vaping products. Furthermore, an information update to the general Canadian population warning of the potential risk of VALI in September 2019[30] may have encouraged self-regulating behaviours such as refraining from using illicit products and discontinuing the use of vaping products if feeling sick. Further research and surveillance are needed to understand the effect of this messaging on behavioural change.

Strengths and limitations

Our study exploring the trends in VALI cases in Canada contributes to the evidence base and consequently to improved understanding of severe vaping-related harms and the clinical management of suspected VALI cases.

However, our results should be viewed in light of certain limitations. The small sample size (20 cases) and limited case histories of patients in the study limited the analyses and interpretation of results, making it difficult to identify a particular risk factor. The data may be subject to reporting biases from patients, their families and health care providers, as most were collected retrospectively and some patients could not remember the products used. Individuals may have been hesitant to disclose use of cannabis-containing vaping products, given these products were illegal in the Canadian marketplace until December 2019, fearing the stigma of using illegal products and the repercussions of admitting use. Due to the small sample of products tested by HC-ROEB-Laboratories and HC-HECSB-PSL, the results of the laboratory tests should not be interpreted as identified causes of VALI. Furthermore, no bronchoalveolar lavage samples were tested for Canadian cases, which was a key factor in identifying vitamin E acetate in the US investigation. Underreporting of cases and vaping behaviours likely occurred in a similar extent in both Canada and the US.

VALI is a diagnosis of exclusion and its symptoms may occur along a spectrum. Patients who presented to emergency departments with mild symptoms and/or whose symptoms resolved with outpatient interventions may be underreported or not identified. Without a baseline, it is difficult to know if rates of VALI-like presentations differ as a function of frequency and duration of use, which cannot be known from counts among vaping patients alone. Given the prevalence of vaping in the population in Canada, especially among youth, and the nonspecific nature of the case definition and symptom presentation, the possibility that vaping is coincidentally associated with VALI in at least some cases cannot be excluded. Additionally, with more than half of the cases classified as probable, some caution must be exercised regarding misdiagnosis and confounders; patients with respiratory infections or other conditions causing infiltrates may have been captured as VALI due to a vaping history that may not have been related to their symptoms.

Furthermore, more than two-thirds of VALI patients reported prior or current use of combustible tobacco or cannabis or both, thus exposing these patients to lung damage potentially unrelated to vaping. Many also reported pre-existing conditions that may have affected lung function and contributed to greater severity of illness in certain cases. Since February 2020, when the COVID-19 epidemic began in Canada, probable or confirmed COVID-19 cases could have confounded potential VALI cases, given the overlap of symptoms and disease progression.[31] While provinces and territories continue to monitor for and report on VALI cases, the de-escalation of active surveillance of VALI due to COVID-19 transmission in Canada may have contributed to underreporting of cases since March 2020.

Conclusion

While vaping is generally considered to lead to lower exposure to known toxicants than combustible smoking, there are still many unknowns about vaping of substances, and it is not without risks. VALI was detected in Canada between September 2019 and December 2020; however, it was at a much lower rate and possibly through a differing mechanism than EVALI in the US. Unlike in the US, where vitamin E acetate was identified as a novel adulterant in cannabis-containing products obtained from informal sources, it was not identified in sufficient amounts in any products tested related to VALI cases in Canada. Although nicotine products were reported to have been used by the majority of VALI patients and detected in several product samples, a causal relationship cannot be assumed at this time. No single

causative agent responsible for VALI could be identified.

As the prevalence of using nicotine and cannabis-containing vaping products increases in Canada, especially among youth who have previously never smoked, additional research is needed to clarify how changing patterns of vaping product use, including the frequency and intensity of use, may contribute to acute and chronic harms, including VALI, nicotine or cannabis addiction and future smoking trends. In addition, continuing education to primary care physicians, emergency department clinicians and other primary care or outpatient health care providers (e.g. nurse practitioners) is important to maintain awareness of VALI as a potential diagnosis.

The factors influencing VALI in Canada are likely complex and multifactorial. While evidence is lacking in this area, it is important to investigate both the short- and long-term health effects of nicotine and cannabis vaping, including the possible influence on susceptibility to infectious diseases. Maintaining awareness and vigilance for the detection and reporting of VALI cases by health care providers is important to capture a complete picture of VALI in Canada and better characterize factors influencing VALI.

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Conflicts of interest

The authors have no conflicts of interest to disclose.

Authors' contributions and statement

MB, LB and SOC contributed to the study conception and design. Material preparation, data acquisition, analysis and interpretation were performed by MB and TP. The first draft of the manuscript was written by MB and TP with comments from all authors. All authors read and approved the final manuscript.

The content and views expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

References

1. Government of Canada. Canadian Tobacco, Alcohol and Drugs Survey (CTADS): summary of results for 2017 [Internet]. Ottawa (ON): Government of Canada; 2019 [modified 2021 Aug 12; cited 2021 Sept 28]. Available from: https://www.canada.ca/en/health-canada/services/canadian-tobacco-alcohol-drugs-survey/2017-summary.html

2. Government of Canada. Canadian Tobacco and Nicotine Survey (CTNS): summary of results for 2019 [Internet]. Ottawa (ON): Government of Canada; 2020 [cited 2020 Jul 7]. Available from: https://www.canada.ca/en/health-canada/services/canadian-tobacco-nicotine-survey/2019-summary.html#n4

3. Government of Canada. Summary of results for the Canadian Student Tobacco, Alcohol and Drugs Survey 2018-19 [Internet]. Ottawa (ON): Government of Canada; 2019 [cited 2021 Sep 28]. Available from: https://www.canada.ca/en/health-canada/services/canadian-student-tobacco-alcohol-drugs-survey/2018-2019-summary.html

4. National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on the Review of the Health Effects of Electronic Nicotine Delivery Systems. Public health consequences of e-cigarettes. Washington (DC): National Academies Press; 2018. 774 p.

5. Christiani DC. Vaping-induced acute lung injury. N Engl J Med. 2020; 382(10):960-2. https://doi.org/10.1056/NEJMe1912032

6. Muthumalage T, Friedman MR, McGraw MD, Ginsberg G, Friedman AE, Rahman I. Chemical constituents involved in e-cigarette, or vaping product use-associated lung injury (EVALI). Toxics. 2020;8(2):25. https://doi.org/10.3390/toxics8020025

7. Layden JE, Ghinai I, Pray I, et al. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin — final report. N Engl J Med. 2020; 382(10):903-6. https://doi.org/10.1056/nejmoa1911614

8. Maddock SD, Cirulis MM, Callahan SJ, et al. Pulmonary lipid-laden macrophages and vaping. N Engl J Med. 2020;381(15):1488-9. https://doi.org/10.1056/nejmc1912038

9. Henry TS, Kanne JP, Kligerman SJ. Imaging of vaping-associated lung disease. N Engl J Med. 2019; 381(15):1486-7. https://doi.org/10.1056/nejmc1911995

10. Landman ST, Dhaliwal I, Mackenzie CA, Martinu T, Steele A, Bosma KJ. Life-threatening bronchiolitis related to electronic cigarette use in a Canadian youth. CMAJ. 2019;191(48): E1321-E1331. https://doi.org/10.1503/cmaj.191402

11. Centers for Disease Control and Prevention (CDC). Outbreak of lung injury associated with the use of e-cigarette, or vaping, products [Internet]. Atlanta (GA): CDC; 2020 [reviewed 2021; cited 2021 Sep 28]. Available from: https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html

12. Friedman AS. Association of vaping-related lung injuries with rates of e-cigarette and cannabis use across US states. Addiction. 2021;116(3):651-7. https://doi.org/10.1111/add.15235

13. Chatham-Stephens K, Roguski K, Jang Y, et al. Characteristics of hospitalized and nonhospitalized patients in a nationwide outbreak of e-cigarette, or vaping, product use-associated lung injury – United States, November 2019. MMWR Morb Mortal Wkly Rep. 2019;68(46):1076-80. https://doi.org/10.15585/mmwr.mm6846e1

14. Taylor J, Wiens T, Peterson J, et al. Characteristics of e-cigarette, or vaping, products used by patients with associated lung injury and products seized by law enforcement – Minnesota, 2018 and 2019. MMWR Morb Mortal Wkly Rep. 2019; 68(47):1096-1100. https://doi.org/10.15585/mmwr.mm6847e1

15. Pray IW, Atti SK, Tomasallo C, Meiman JG. E-cigarette, or vaping, product use-associated lung injury among clusters of patients reporting shared product use – Wisconsin, 2019. MMWR Morb Mortal Wkly Rep. 2020;69(9):236-40. https://doi.org/10.15585/mmwr.mm6909a4

16. Heinzerling A, Armatas C, Karmarkar E, et al. Severe lung injury associated with use of e-cigarette, or vaping, products—California, 2019. JAMA Intern Med. 2020;180(6):861-9. https://doi.org/10.1001/jamainternmed.2020.0664

17. Blount BC, Karwowski MP, Morel-Espinosa M, et al. Evaluation of bronchoalveolar lavage fluid from patients in an outbreak of e-cigarette, or vaping, product use-associated lung injury - 10 states, August–October 2019. MMWR Morb Mortal Wkly Rep. 2019;68(45):1040-1. https://doi.org/10.15585/mmwr.mm6845e2. Erratum in: MMWR. 2020;69:116. https://doi.org/10.15585/mmwr.mm6904a6

18. Blount BC, Karwowski MP, Shields PG, et al. Vitamin E acetate in bronchoalveolar-lavage fluid associated with EVALI. N Engl J Med. 2020; 382(8):697-705. https://doi.org/10.1056/nejmoa1916433

19. U.S. Food and Drug Administration. Lung illnesses associated with use of vaping products: information for the public, FDA actions, and recommendations [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; 2020. Available from: https://www.fda.gov/news-events/public-health-focus/lung-illnesses-associated-use-vaping-products#Analysis

20. Ghinai I, Navon L, Gunn JKL, et al. Characteristics of persons who report using only nicotine-containing products among interviewed patients with e-cigarette, or vaping, product use-associated lung injury – Illinois, August–December 2019. MMWR Morb Mortal Wkly Rep. 2020;69(3):84-9. https://doi.org/10.15585/mmwr.mm6903e1

21. Government of Canada. Tobacco and Vaping Products Act [Internet]. Ottawa (ON): Government of Canada; 2018. Available from: https://www.canada.ca/en/health-canada/services/health-concerns/tobacco/legislation/federal-laws/tobacco-act.html

22. Government of Canada. Canada Consumer Product Safety Act (S.C. 2010, c. 21) [Internet]. Ottawa (ON): Government of Canada; 2020 [modified 2021 Aug 25; cited 2021 Sep 28]. Available from: https://laws-lois.justice.gc.ca/eng/acts/c-1.68/

23. Government of Canada. Cannabis legalization and regulation [Internet]. Ottawa (ON): Government of Canada; 2019 [modified 2021 Jul 07; cited 2021 Sep 28]. Available from: https://www.justice.gc.ca/eng/cj-jp/cannabis/

24. Wing C, Bradford AC, Carroll AE, Hollingsworth A. Association of state marijuana legalization policies for medical and recreational use with vaping-associated lung disease. JAMA Netw Open. 2020;3(4):e202187. https://doi.org/10.1001/jamanetworkopen.2020.2187

25. Canada Border Services Agency. Memorandum D19-9-2: importation and exportation of cannabis, controlled substances and precursors [Internet]. Ottawa (ON): Government of Canada; 2018 [cited 2021 Sep 28]; Available from: https://cbsa-asfc.gc.ca/publications/dm-md/d19/d19-9-2-eng.html

26. Eubank S, Guclu H, Kumar VS, et al. Modelling disease outbreaks in realistic urban social networks. Nature. 2004;429(6988):180-4. https://doi.org/10.1038/nature02541

27. Cauchemez S, Boëlle PY, Donnelly CA, et al. Real-time estimates in early detection of SARS. Emerg Infect Dis. 2006;12(1):110-3. https://doi.org/10.3201/eid1201.050593

28. Institute of Medicine (US) Forum on Microbial Threats. Global infectious disease surveillance and detection: assessing the challenges—finding solutions, workshop summary. Washington (DC): National Academies Press; 2007. 284 p.

29. Pan-Canadian Public Health Network (PHN). About the Pan-Canadian Public Health Network [Internet]. Ottawa (ON): PHN; 2020 [cited 2021 Sep 28]. Available from: http://www.phn-rsp.ca/network-eng.php#:~:text=The%20Council%20of%20Chief%20Medical,knowledge%2C%20experience%20and%20best%20practices

30. Government of Canada. Information update—Health Canada warns of potential risk of pulmonary illness associated with vaping products [Internet]. Ottawa (ON): Government of Canada; 2019 [cited 2021 Sep 28]. Available from: https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2019/70919a-eng.php

31. Armatas C, Heinzerling A, Wilken JA. Notes from the field: e-cigarette, or vaping, product use-associated lung injury cases during the COVID-19 response – California, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(25): 801-2. https://doi.org/10.15585/mmwr.mm6925a5